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CHAPTER 4

Treatment of Depression in Patients with Diabetes: Efficacy, Effectiveness and Maintenance Trials, and New Service Models

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Two systematic reviews have found rates of major depression to be between 12 and 17% in patients with diabetes [1, 2]. These rates have been shown to be twofold higher than those of medical controls [1, 2]. Patients with comorbid major depression and diabetes, compared to those with diabetes alone, have been shown to have a higher medical symptom burden [3], more decrements in functioning and quality of life [4], higher medical costs [5], poor self-care (i.e. adherence to diet, exercise, cessation of smoking recommendations and disease control medication) [6], poorer glycaemic control [7], an increased number

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of Framingham risk factors for cardiovascular disease [8], and an increased risk of macrovascular and microvascular complications and mortality [9–11].

Depression tends to be either a chronic or a recurrent condition in patients with diabetes. Data from a large study of over 4800 patients with diabetes enrolled in a health maintenance organization (HMO) found that approximately 70% of those with comorbid depression (based on scoring $\geq$10 on the Patient Health Questionnaire-9) had experienced affective symptoms for two years or longer [12]. Among mixed-aged depressed patients without diabetes in this same health maintenance organization, only approximately 20% described two or more years of affective symptoms [13]. The increase in chronicity of depression is, at least in part, age related. Patients with diabetes tend to be older, and recent primary care data have shown that the average length of an episode of depression in older primary care patients is approximately 18 months [14], whereas in mixed-aged populations the mean length of an episode is approximately 4–6 months [15].

The tendency for depressive symptoms to be chronic in patients with diabetes is also shown by recent data from a five-year follow-up study of approximately 2700 patients with diabetes. Approximately 82% of patients who met DSM-IV criteria for major depression at five-year follow-up had minor or major depression at baseline [16]. Finally, the recurrent course of depression was shown in a longitudinal study, which found that 79% of patients with diabetes who had major depression relapsed over a five-year follow-up period, with a mean of four episodes per patient [17].

A recent large European study showed that over 50% of community respondents with anxiety and depressive disorders were not receiving healthcare services for their psychiatric illness, whereas only 8% of respondents with diabetes reported no use of services for their medical condition [18]. Thus, the current unmet need for mental health care is significantly higher than the unmet need for medical care. Given that the vast majority of patients with diabetes are receiving regular medical care, it is possible that patients with comorbid depression and diabetes would receive more accurate diagnosis and effective treatment for depression than those with depression alone. However, in a large United States population-based sample, over a 12-month period, only approximately 51% of patients with major depression and

diabetes were accurately recognized by the healthcare system [19]. Factors associated with higher recognition rates included female gender, comorbid dysthymia or panic attacks, the patient's perception of poor health, and making more than seven primary care visits per year [19]. Among those whose depression was accurately diagnosed, there were deficits in quality of care, with 43% receiving one or more antidepressant prescriptions and only 6.7% receiving four or more sessions of psychotherapy during the 12-month period [19]. The likelihood is that patients with fee-for-service medical insurance in the United States would have even lower rates of detection and provision of guideline-level depression care, due to more financial, geographic and organizational barriers to mental health care.

Given the high prevalence and chronicity of depression in patients with diabetes and the adverse impact of depression on functioning, quality of life and medical outcomes, the provision of evidence-based depression treatment is of great public health importance. This chapter focuses on: (a) whether research-proven pharmacotherapies and psychotherapies are efficacious in patients with comorbid depression and diabetes; (b) the development and testing of primary care-based health services models to improve detection and quality of depression care for this population; and (c) the evidence about maintenance depression treatment.

Steps are also described to enhance diagnosis and engagement of patients with diabetes in depression treatment as well as the necessary changes in primary care systems needed to enhance early accurate diagnosis and provision of evidence-based treatments for affective illness. Finally, new research models that combine care management for depression with care management to improve glycaemic, lipid and blood pressure control in patients with diabetes and/or heart disease are described.

EFFICACY STUDIES

Most large treatment studies have found that medical illness and decrements in physical functioning are associated with lower rates of response to evidence-based depression treatments [20]. Patients with diabetes frequently develop complications of their illness that lead to

decrements in functioning, such as neuropathy, peripheral ulcers and amputation. Recent US Medicare data have shown that approximately 70% of patients with diabetes have four or more comorbid medical conditions and these patients with multiple conditions often have the most deficits in functioning and high rates of comorbid depression [21]. Therefore, an important question for researchers and clinicians is whether evidence-based pharmacotherapies and psychotherapies that have proven effective in populations of patients with depression with minimal medical illness would be as efficacious in patients with diabetes.

Several systematic reviews have been completed exploring effect sizes of psychotherapeutic as well as pharmacological treatments of patients with comorbid depression and diabetes [22, 23]. Efficacy trials generally evaluate intensive treatment of a carefully selected patient group by highly trained staff. Patients with clinically significant psychiatric comorbidities, such as panic disorder or medical comorbidities, are often excluded from these trials.

A systematic review of efficacy trials performed in 2009 yielded 11 randomized clinical trials, five on psychotherapeutic interventions and six on pharmacological treatments [24–34]. The results of this review are shown in Table 4.1. Most trials were small, with only one recruiting more than 100 patients and the others including 60 or fewer patients. Most trials were completed on patients with type 2 diabetes with serious depressive symptoms or major depressive disorder, and effect sizes were specified for depressive symptom severity as well as for glycaemic control.

The results were presented in terms of standardized effect sizes (Cohen's *d*). These effect sizes indicate by how many standard units the intervention group is better off than the control group on a depression severity scale. The effect size (*d*) is usually calculated by subtracting the average score of the control group from the average score of the experimental group and dividing the raw difference score by the pooled standard deviation of the experimental and control group [35]. An effect size of 0.5 thus indicates that the mean of the experimental group is half a standard unit larger than the mean of the control group. It is generally assumed that an effect size of 0.56–1.2 represents a large clinical effect,

Table 4.1 Efficacy trials of psychotherapeutic and pharmacological treatments for depression in patients with diabetes

Study	N (completers); diabetes type; mean age	Intervention conditions; follow-up (FU)	Outcome assessment (depression; diabetes, DM)	Effect size (depression; diabetes, DM)	Comments
Psychotherapeutic interventions (N = 310)					
Lustman *et al.*, 1998 (USA) [24]	N = 41; 100% type 2; 53.1–56.4 ± 10.5–9.7	CBT plus diabetes education versus diabetes education alone FU: 11 wk, 6 mo	*Depression:* Response (reduction BDI ≥ 50%) $p < 0.001$ in CBT group *DM:* HbA1c lower in CBT group, $p < 0.03$	*Depression:* Δ −1.112 *DM:* Δ −0.704	Improvement in depression as well as glycaemic control in CBT group
Huang *et al.*, 2002 (China) [25]	N = 59; 100% type 2; N/A	Antidiabetics + diabetic education + psychological treatment + relaxation and music treatment vs antidiabetics only FU: 3 mo	*Depression:* SDS total score difference in means 0.07, $p < 0.05$ *DM:* HbA1c difference in means 1.7, $p < 0.05$	*Depression:* Δ −0.521 *DM:* Δ −0.521	Improvement in depression as well as glycaemic control in group treated with psychotherapy

(*Continued*)

Table 4.1 *(Continued)*

Study	N (completers); diabetes type; mean age	Intervention conditions; follow-up (FU)	Outcome assessment (depression; diabetes, DM)	Effect size (depression; diabetes, DM)	Comments
Li *et al.*, 2003 (China) [26]	N = 120; N/A; 50.5–52.3 ± 10.4–11.2	Antidiabetics + diabetic education + psychological treatment vs antidiabetics only FU: 4 wk	*Depression:* SDS total score difference in means 13.4, $p < 0.01$ *DM:* FBG difference in means 2.09, $p < 0.05$	*Depression:* Δ −0.478 *DM:* Δ −0.362	Anxiety (SAS ≥ 50) taken into account as well. Improvement in depression as well as glycaemic control in group treated with psychotherapy
Lu *et al.*, 2005 (China) [27]	N = 60; 100% type 2; 65.6–64.9 ± 9.8–9.5	Diabetes and CVA education + electromyographic treatment + psychological treatment vs usual care FU: 4 wk	*Depression:* HAMD-17 total score difference in means 7.3, $p < 0.01$ *DM:* difference in means FPG 1.54, $p < 0.05$	*Depression:* Δ −0.688 *DM:* Δ −0.517	Hemiplegia after CVA as DM complication. Improvement in depression as well as glycaemic control in group treated with psychotherapy

Simson *et al.*, 2008 (Germany) [28]	N = 30; 80% Type 2; 60.5 ± 10.9	Individual supportive psychotherapy vs usual care FU: discharge (3–20 wk)	*Depression* HADS depression scale total score mean difference 1.9, $p = 0.018$ *DM:* PAID mean difference 7.6, $p = 0.008$	*Depression:* Δ −0.918 *DM:* Δ −1.043	Diabetic foot as DM complication. Improvement in depression as well as glycaemic control in supportive psychotherapy group
Pharmacological interventions (N = 215)					
Lustman *et al.*, 1997 (USA) [29]	N = 28; 50% type 2; 49.0–49.2 ± 12.1–13.7	Glucometertraining + nortriptyline vs placebo FU: 9 wk	*Depression:* BDI total score, mean difference 5.6, $p = 0.03$ *DM:* HbA1c, no significant difference, no outcome reported	Depression: Δ −0.868 *DM:* Δ 0	Poorly controlled (HbA1c ≥9%) as inclusion criterion. Improvement in depression but not in glycaemic control in nortriptyline vs control. Nortryptiline may have negative impact on glycemic control.

(Continued)

Table 4.1 (*Continued*)

Study	N (completers); diabetes type; mean age	Intervention conditions; follow-up (FU)	Outcome assessment (depression; diabetes, DM)	Effect size (depression; diabetes, DM)	Comments
Lustman *et al.*, 2000 (USA) [30]	N = 54; 55.6% type 2; 45.0–47.7 ± 13.0–11.5	Fluoxetine vs placebo FU: 8 wk	*Depression:* HAMD total score mean difference 26.7, $p < 0.04$ *DM:* HbA1c mean difference 0.33, $p = 0.13$ (n.s.)	*Depression:* Δ −0.573 *DM:* Δ 0.419	Improvement in depression but not in glycaemic control in fluoxetine vs placebo.
Paile-Hyvärinen *et al.*, 2003 (Finland) [31]	N = 13; 100% type 2; 61.1–62.3 ± 8.6–11.5	Paroxetine vs placebo FU: 4 wk	After initial improvement in paroxetine group at 3 mo, no significant improvement for both outcomes at end of follow-up. *Depression:* MADRS total score mean difference 2.50, $p = 0.25$ (n.s.)	*Depression:* Δ −0.676 *DM:* Δ 1.073	Poorly controlled (HbA1c ≥6.5% or FBG ≥7.0) as inclusion criterion. Probably a combination of ceiling effect and underpowered study.

			DM: GHbA1c mean difference 0.37, $p = 0.08$ (n.s.)		
Xue *et al.*, 2004 (China) [32]	N = 48; 85.4% type 2 ; 21–65	Paroxetine vs placebo FU: 8 wk	*Depression:* HAMD-17 total score mean difference 5.7, $p < 0.01$ *DM:* HbA1c mean difference 0.4, $p = 0.245$ (n.s.)	*Depression:* Δ−0.776 *DM:* Δ 0.340	Improvement in depression but not in glycaemic control in paroxetine vs placebo.
Gülseren *et al.*, 2005 (Turkey) [33]	N = 23; 100% type 2; 58.2–57.1 ± 12.3–10.4	Fluoxetine vs paroxetine FU: 12 wk	Both groups improved significantly in depression (HDRS mean difference 0.62, $p = 0.003$) but not in HbA1c (mean difference 0.11, n.s.)		No significant difference between the two conditions.

(*Continued*)

Table 4.1 (*Continued*)

Study	N (completers); diabetes type; mean age	Intervention conditions; follow-up (FU)	Outcome assessment (depression; diabetes, DM)	Effect size (depression; diabetes, DM)	Comments
Paile-Hyvärinen *et al.*, 2007 (Finland) [34]	N = 49; 100% type 2; 59.5–59.2 ± 6.0–5.4	Paroxetine vs placebo FU: 3 mo, 6 mo	*Depression:* HADS depression scale total score mean difference 0.7, p = 0.448 (n.s.) *DM:* GHbA1c mean difference 0.13, p = 0.693 (n.s.)	*Depression:* Δ −0.260 *DM:* Δ 0.135	No significant improvement in depressive outcomes and glycaemic control.

DM – diabetes; CBT – cognitive behavioural therapy; SDS – Self Rating Depression Scale; SAS – Zung Self Rating Anxiety Scale; HAMD-17 – Hamilton Depression Rating Scale – 17; FPG – fasting plasma glucose; CVA – cerebrovascular accident; HADS – Hospital Anxiety and Depression Scale; PAID – Problem Areas in Diabetes Survey; BDI – Beck Depression Inventory; MADRS – Montgomery–Asberg Depression Rating Scale; n.s. – not significant; N/A – not available.

while effect sizes of 0.33–0.55 are moderate and effect sizes of 0–0.32 are small [36].

As can be seen in Table 4.1, the effect sizes of the psychotherapeutic interventions were moderate to large for improvement of depressive symptoms, and moderate to large for improvement of glycaemic control. In a meta-analysis, the effect sizes of the psychotherapeutic trials were pooled. The pooled estimate of the psychotherapeutic trails was −0.645 (95% CI −0.874; −0.415) for depression outcomes, and −0.477 (95% −0.715; −0.239) for glycaemic control. Three of the five psychotherapy trials compared an evidence-based depression psychotherapy and diabetes education to diabetes education alone. Therefore, it is unclear whether improvements in glycaemic control were due to the beneficial effect of the depression-focused psychotherapy or the combination of both depression therapy and diabetes education.

As shown in Table 4.1, the pharmacotherapeutic interventions (all but one evaluated the efficacy of selective serotonin reuptake inhibitors, SSRIs) had moderate effects on depressive symptoms, and small effects on glycaemic control. The pooled estimate of the pharmacotherapeutic trials, of which only one (the Lustman study) included a direct intervention to improve glycaemic control, was −0.615 (95% CI −0.916, −0.313) for depression outcomes and −0.376 (95% −0.701;−0.052) for glycaemic control. The effect on depressive outcomes was very similar, but the effect on glycaemic control was smaller than that of the psychotherapeutic studies, many of which had explicit interventions aimed at improving glycaemic control. The pharmacologic trials were also small, with 13 to 54 patients enrolled. The small numbers of patients enrolled in both psychotherapy and pharmacologic efficacy trials limits the generalizability of the findings.

In terms of public health, the findings from the psychotherapy and pharmacotherapy trials suggest that, in order to improve self-care and glucose control in patients with diabetes and depression, simple treatment of the comorbid depressive disorder is likely to be insufficient. To improve both psychiatric and medical outcomes, a more comprehensive approach that includes both evidence-based depression treatment and interventions aimed at improving diabetes self-care and glucose control is likely to be needed.

EFFECTIVENESS TRIALS: COLLABORATIVE DEPRESSION CARE

A key concept involved in the development of primary care-based models to improve care of chronic illnesses is population-based care [37]. This is an approach to planning and delivering care to defined patient populations which tries to ensure that effective interventions reach all patients that need them (i.e. all patients with diabetes who have comorbid major depression and/or dysthymia) [37]. This model often requires depression screening and a team approach to care rather than infrequent brief visits with a primary care physician. The model was developed to overcome the gaps in depression treatment experienced by patients with diabetes, with only 50% being accurately diagnosed and only half of these receiving even a minimal standard of pharmacologic or psychotherapeutic treatments [37].

Collaborative care is a population-based health services model that was developed to increase exposure of patients with depression in primary care systems to evidence-based depression pharmacologic care and psychotherapies [37]. The key components of collaborative care include: enhanced patient education using videotapes, pamphlets and books; integration of allied health professionals into primary care systems to track depression outcomes, side effects and adherence and to provide support for behavioural change; use of a monitoring tool such as the Patient Health Questionnaire – 9 (PHQ-9) [38] and an electronic disease register; caseload supervision by a psychiatrist; and stepped care approaches. Stepped care involves increasing the intensity of care based on persistent depressive symptoms.

In a study in The Netherlands, psychiatric consultation was found to facilitate implementation of stepped care for depressed patients [39]. A similar positive effect of psychiatric caseload supervision of the allied health professional who provided collaborative care was established in a meta-analytic review of 37 trials [40]. Thus, in a stepped care approach, if a patient initiates treatment with an evidence-based psychotherapy and remains depressed at 4–6 weeks, an antidepressant may be recommended during psychiatric supervision. Alternatively, if an initial trial of an antidepressant has not led to adequate symptom relief, the medication may be changed or augmented or psychotherapy added. Given the low rates of detection of depression among patients

with diabetes, developing population-based models like collaborative care usually requires methods to screen patients for depression.

There are now three trials of collaborative care versus usual care in patients with depression and diabetes [12, 41, 42]. These studies were developed in distinct populations: mixed-aged patients enrolled in nine primary care clinics of a non-profit HMO [12]; elderly patients (≥65 years of age) in eight systems of care in seven geographic regions of the United States [41]; and mixed-age, mainly Hispanic patients, mostly living below United States poverty levels and attending two large primary care clinics in Los Angeles [42]. In all three trials, the population of patients with diabetes in the primary care systems were screened for depression with a questionnaire and those with major depression and/or dysthymia were then offered randomization to either collaborative care or usual care [12, 41, 42]. These trials included representative patients from the population, only excluding those with terminal medical illness, dementia, or already seeing a psychiatrist. In two of the trials, approximately 50% of the randomized patients were taking an antidepressant but still met criteria for major depression or dysthymia and thus met inclusion criteria for the trial [12, 41].

All three collaborative care interventions offered a choice of starting with antidepressant medication or problem solving therapy (PST) [12, 41, 42]. Care managers worked in a team with the psychiatrist and primary care physician to provide enhanced education about depression, track symptoms, adherence and side effects, provide recommendations about medications to the primary care physicians based on caseload supervision by the psychiatrist, and provide PST. All three trials included a stepped care approach. Thus, if patients chose antidepressant medication as their initial treatment, but did not respond to optimal dosages, their antidepressant would be augmented or changed, or PST could be added. Similarly, if they did not respond to an initial treatment choice of PST, antidepressant medication could be added. These trials were focused on improving quality of care of depression and did not specifically focus on quality of care of diabetes.

All three trials showed significant improvements in quality of depression care compared to the usual care control groups, with improvement in percentage of patients treated with and adhering to

antidepressant medication and the percentage receiving ≥4 sessions of psychotherapy. All three trials also showed improvements in depressive symptoms compared to usual care over the initial 12- to 18-month period [12, 41, 42]. Two of the three trials included a 24-month follow-up and showed continued improvement in depressive symptoms compared to usual care at the 24-month stage (one year after the intervention ended) [12, 41]. Cohen's *d* in terms of improvement of severity of depressive symptoms in the three trials was 0.320, 0.676 and 0.337, which can be considered moderate to large effects. In a meta-analysis, the pooled estimate of Cohen's *d* for the three collaborative care trials was 0.441 (95% CI −0.644; −0.251).

Two of the three trials also showed improvement compared to usual care in physical functioning and quality of life over the initial 12- to 18-month period [12, 41, 42]. Thus, enhancing the quality of depression care appears to be an effective way to decrease physical decline in these aging medically ill populations. However, none of the three trials showed improvement in the collaborative care intervention group compared to the usual care controls in most components of self-care (i.e. adherence to checking blood glucose, diet, cessation of smoking, or taking disease control medication as prescribed) or mean HbA_{1c} levels [12, 41–43]. These data are supported by several large trials of enhancing treatment of depression in patients with post-myocardial infarction, which have shown improvements in quality of depression care and depression outcomes, but not in cardiac complications or mortality [44, 45].

Two of the three collaborative care trials have completed cost-effectiveness analyses. These trials have shown that collaborative care versus usual primary care was associated with significant increments in depression-free days over a two-year period, that is, a total of 61 (95% CI 11, 82) and 115 (95% CI 72, 159) depression-free days, respectively [46, 47]. Both trials also showed that the (US)$500–700 increased mental health costs associated with the collaborative care intervention were offset by greater savings in total medical costs (Figure 4.1) [46, 47]. The medical cost savings were largely in year 2, emphasizing the importance of examining at least two years of healthcare cost data in these trials. Both trials showed a high probability that collaborative care was a 'dominant' intervention, defined as a medical intervention that is more effective and is

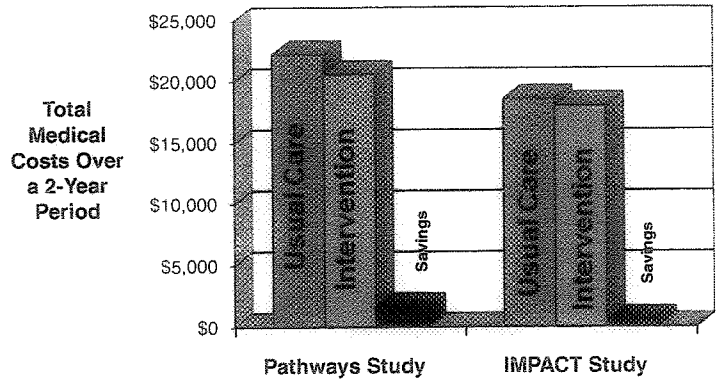

Figure 4.1 Healthcare costs of usual and collaborative (enhanced) care over a two-year period.

associated with medical cost savings [46, 47]. One of these trials also continued to track medical costs over a five-year period and found that the same trends for cost savings continued in years 3–5 in the intervention group compared to controls [48]. This suggests that enhancing depression care and outcomes in patients with depression and diabetes may place patients on a different long-term medical cost trajectory.

MAINTENANCE TRIALS

Given the high rates of relapse and chronicity in patients with depression and diabetes that are described above, researchers have begun to test the effect of maintenance antidepressant treatment.

A recent maintenance trial randomized 152 patients who had recovered with an open label trial of sertraline to either sertraline or placebo for up to 52 weeks [49]. Patients who received maintenance treatment with the SSRI had a significantly greater depression-free interval compared to those treated with placebo (median time to recurrence was 57 days in the placebo group compared to 226 days in the patients treated with sertraline) [49]. There were no significant differences in glycaemic control between sertraline and placebo in this maintenance phase of treatment. However, both depression recovery

with the SSRI as well as sustained remission with or without active treatments were associated with improvements in HbA_{1c} levels for at least one year [49].

A second maintenance trial that treated 93 patients with type 2 diabetes with acute phase bupropion offered maintenance treatment with this medication to patients who remitted (N = 63) at the dosage that was associated with remission [50]. Body mass index (BMI), total fat mass and HbA_{1c} values decreased significantly and composite diabetes care improved over the initial acute phase, and these effects persisted through the maintenance phase. Reduction in both BMI and depression severity with bupropion treatment predicted lower HbA_{1c} levels after acute phase therapy, but only a reduction in depression predicted lower HbA_{1c} levels during the maintenance phase of treatment [50].

The first two trials of collaborative care included a session of relapse prevention for patients who were nearing completion of the one-year intervention [12, 41]. The relapse prevention session included a review with the patient about prodromal symptoms (i.e. symptoms that are harbingers that they may be having relapse of depression) and strategies to cope with relapse, such as calling their primary care physician. The relapse prevention sessions also included stress reduction techniques the patient would regularly engage in, such as exercise and recommendations about maintenance antidepressant treatment or referral for more intensive psychotherapy. Both of these collaborative care trials showed that intervention patients were continuing to experience significantly less depressive symptoms compared to usual care controls one year after completing the 12-month trial [12, 41].

NEW TREATMENT MODELS

Piette *et al.* [51] have proposed a model to explain how depression treatment may improve the outcomes of comorbid chronic disease, which they applied to diabetes. An adaptation of this model to indicate reciprocal adverse effects of comorbid chronic disease and depressive illness is described in Figure 4.2. In this model, effective treatment of depression may be more difficult because of the adverse health

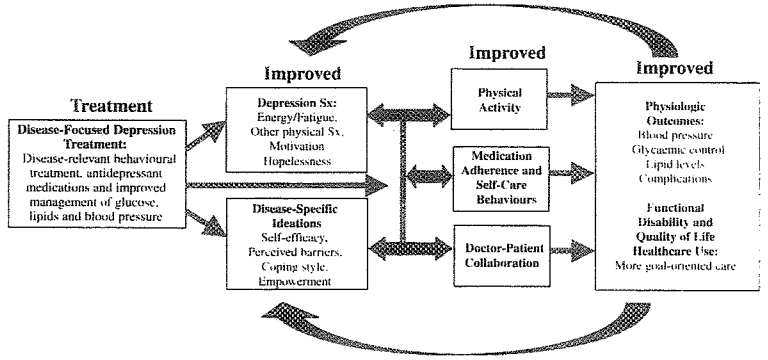

Figure 4.2 Adaptation of Piette's model linking depression and chronic disease outcomes. Reproduced with permission from Intellisphere, LLC

behaviours (smoking, obesity, sedentary lifestyle, lack of adherence to disease control medications) as well as higher symptom burden and functional disability associated with depression. Adverse health behaviours do not necessarily improve with effective depression treatment alone, and may be negative prognostic factors for depression outcomes (e.g. obesity is associated with negative social feedback, lower self-esteem and less exercise, which all effect mood). Sedentary lifestyle has been shown in prospective studies to be associated with subsequent development of depression [52]. Depression may also lead to poor self-care, resulting in a higher risk of diabetic macrovascular and microvascular complications, which in turn cause functional decrements which can precipitate a new episode or relapse of depression.

New treatment models (termed 'disease-focused depression treatment' in Figure 4.2) that focus on improving quality of both depression and medical treatment may be needed, which will emphasize improving depression treatment, increasing positive health behaviours (exercise and diet) and improving disease control of chronic medical illness by optimizing medication adherence and treatment in order to avoid complications. Several ongoing studies are testing these combined psychiatric and medical interventions in patients with diabetes and depression and those with diabetes and/or coronary heart disease and depression [53].

IMPROVING DEPRESSION CARE IN INDIVIDUAL PATIENTS WITH DIABETES

Table 4.2 describes a clinical approach to assessing and treating depression and other psychiatric disorders in patients with diabetes [54]. Because of the high prevalence and adverse impact depression has in patients with diabetes, it is recommended that patients be screened for depression at least once a year with a tool such as the PHQ-9. The physician should have a high index of suspicion of a depression diagnosis in patients with poor control of blood glucose, poor adherence to self-care, pain and other somatic complaints and those who elicit frustration in the doctor–patient relationship. The PHQ-9 not only provides a probable diagnosis of major depression for those scoring $\geq$10, but also includes a 0–27 severity score. This is an ideal scale for gauging success of treatment, and inclusion of the nine key symptoms of depression allows the practitioner to target treatment to specific symptoms, such as insomnia.

In a review, Gilbody *et al.* [55] found that screening for depression is effective if aimed at finding patients with sufficient severity of depressive symptoms to warrant treatment, and if appropriate treatment is subsequently offered as result of such a screening outcome. A similar outcome was found for combined screening for anxiety and depression [56]. Therefore, it is important to embed depression screening in a comprehensive treatment approach such as collaborative care.

Patients with depression and diabetes are frequently frustrated and demoralized and often present with physical symptoms. Depression is actually a better predictor of diabetes symptom reporting than is the level of HbA_{1c} or the number of diabetes complications [3]. Patients are often uncertain about whether their diabetes and physical symptoms are causing depression or vice versa. They often feel resignation and guilt about not being able to manage their diabetic condition. Validating their sense of loss of control of their diabetes in a non-judgmental manner often allows the clinician to improve rapport and engagement [54]. It also offers the clinician the chance to provide education that the patient is experiencing two clinical diseases that can adversely impact each other and that both can be effectively treated. It is helpful to describe the maladaptive physical effects depression can have on medical symptom burden and diabetes control and to explore

Table 4.2 Improving depression care in patients with diabetes

STEP 1 - Screen for:

Depression with PHQ-9
Helplessness/'giving up' or sense of being overwhelmed about disease self-management
Comorbid panic attacks and PTSD with GAD-7
Inability to differentiate anxiety symptoms from diabetes symptoms (e.g. hypoglycaemia)
Associated eating concerns
Emotional eating in response to sadness/loneliness/anger
Binge eating/purging
Night eating

STEP 2 - Improve self-management

Explore 'loss of control' of disease self-management
Explore understanding of bidirectional link between stress and suboptimal disease self-management and outcomes
Define depression and how it overlaps with and is distinct from 'stress'
Review symptoms of depression and how these symptoms overlap with or mimic diabetes symptoms
Discuss depression-related medical symptom amplification
Break down tasks in self-management of diabetes, depression, heart disease, other illnesses
Help patient prioritize order of importance of specific tasks

STEP 3 - Support

Consider adjunctive brief psychotherapy for:
emotional eating (CBT)
breaking down problems (problem solving therapy)
improving treatment adherence (motivational interviewing)

STEP 4 - Consider medication

Comorbid depression and anxiety: SSRI or SNRI
Sexual dysfunction: use bupropion or if already responding to SSRI add buspirone 15 mg BID or bupropion SR 100 mg BID
Significant neuropathy: choose bupropion, venlafaxine or duloxetine due to effectiveness in treating neuropathic pain

PHQ-9 – Patient Health Questionnaire; PTSD – post-traumatic stress disorder; GAD-7 – Generalized Anxiety Disorder Assessment-7; CBT – cognitive behavioural therapy; SSRI – selective serotonin reuptake inhibitor; SNRI – serotonin-noradrenaline reuptake inhibitor.

how depression is affecting adherence to diet, exercise, checking blood glucose and taking medications as prescribed.

Many patients with depression also have comorbid anxiety disorders such as panic, generalized anxiety and post-traumatic stress disorder (PTSD). These disorders can also occur without comorbid depression and have been shown to maladaptively affect adherence and disease control in patients with diabetes [57, 58]. Therefore, screening for these disorders is also important. The Generalized Anxiety Disorder Assessment – 7 (GAD-7) is a new screening tool that screens for four potential anxiety disorders, that is, panic, PTSD, generalized anxiety disorder and social phobia [59].

Many patients with depressive and anxiety disorders and diabetes also go off diabetic diets and may binge on unhealthy foods when they feel emotionally vulnerable. Patients with diabetes also have higher rates of eating disorders. Carefully reviewing the changes in their dietary patterns associated with these stressful times in their life may help the clinician enhance understanding about the fluctuations in weight and glycaemic control that he/she is observing. Night eating syndrome, where the patient awakens during the night and often binges or snacks on unhealthy foods, has been shown to be associated with poor glucose control and diabetes complications [60]. Using motivational interviewing may help patients identify goals to begin to change dietary habits. Psychotherapy approaches, such as cognitive behavioural therapy, may be helpful for those with eating disorders.

A history of the common psychiatric and medical comorbidities or complications in patients with diabetes may lead to targeted selection of psychiatric medication. For patients with comorbid anxiety disorders, SSRIs and serotonin-noradrenaline reuptake inhibitors (SNRIs) may both help depression and effectively treat anxiety. Many patients with diabetes have sexual dysfunction due to the adverse effects of diabetes on the autonomic nervous and vascular systems. In these patients, bupropion is a reasonable first choice for treating depression because, unlike SSRIs or SNRIs, it does not adversely affect sexual function. For patients with depression and diabetic neuropathy, bupropion, venlafaxine and duloxetine may effectively treat both painful neuropathy and depression.

CHANGES IN PRIMARY CARE SYSTEMS NECESSARY TO IMPROVE OUTCOMES OF PATIENTS WITH DEPRESSION AND DIABETES

The American Diabetes Association has now recommended screening for depression in patients with diabetes [61]. This recommendation has developed because of the research documenting the high prevalence of comorbid depression in diabetes and its adverse impact on symptom burden, self-care, functioning and diabetes complications. As reviewed above, valid and reliable screening tools like the PHQ-9 have been developed, but to begin screening requires linking this activity to changes in the primary care system to ensure both patient safety and improved quality of treatment and outcomes. For example, rapid evaluation of patients who score in the severe range on the PHQ-9 (a score of $\geq$20) or those having suicidal ideation on the PHQ-9 is essential. This is similar to running medical tests and ensuring that the primary care system is set up to rapidly respond to a dangerously high laboratory value.

In one clinic that has set up PHQ-9 screening at the University of Washington, a nurse reviews all scores and any patient with a PHQ-9 score $\geq$20 or rating the question about suicide ideation as more than half the days in the prior week receives an immediate social work referral. In collaborative care studies in The Netherlands, the PHQ-9 is monitored every two weeks, and in case of a positive score on the suicide question, the family physician is notified and the consultant psychiatrist consulted according to a protocol embedded in the electronic monitoring system [62, 63].

The collaborative care models that have been shown to improve quality and outcomes of depression patients with diabetes require a team approach. A depression care manager (DCM) and a psychiatrist are the two new members of the team. The DCM provides enhanced patient education about depression and careful tracking of PHQ-9 values, monitors side effects and adherence, and, based on psychiatric caseload supervision, provides recommendations about antidepressant medications to the primary care physician. When the patient continues to have persistent symptoms, the DCM facilitates referral back to the primary care physician or a potential consultation with the psychiatrist or referral for more intensive mental

health screening. In some collaborative care studies, DCMs have also been trained to carry out brief psychotherapy, such as PST, in primary care. Psychiatric supervision of the depression case manager caseload is one of the most cost-effective components of the collaborative care model, because the psychiatrist can often supervise 100–200 cases per year. In some collaborative care models, the psychiatrist may also spend several hours a week evaluating patients with persistent depressive symptoms not improving with DCM and primary care treatment alone.

A key component of this model is either the development of a depression electronic registry to monitor visit dates, PHQ scores and type of treatment provided, or the integration of tracking of PHQ-9 scores into an existing diabetes registry. Many electronic registries have been developed using Access or Excel databases. In a new trial the Seattle research group has developed, termed the TEAMcare trial, PHQ-9 results have been integrated into a diabetes registry that monitors visit dates, LDL, blood pressure and HbA_{1c} results [64].

These newer models of care, like TEAMcare, are using and training diabetes nurses to include depression screening and treatment as an important skill in overall diabetes care. In TEAMcare the diabetes nurses phase in treatment by first enhancing quality of depression care, then focusing on improving quality of care for blood pressure, lipids and glycaemic control, and finally focusing on improving health care behaviours, such as improving diet, increasing exercise, monitoring blood glucose (and, if hypertensive, monitor blood pressure with a home blood pressure device) and increasing other pleasurable activities.

CONCLUSIONS

There is a high prevalence of depressive and anxiety disorders in patients with diabetes, and these disorders adversely affect diabetes self-care, disease control and clinical outcomes. Complications of diabetes resulting in functional impairment can also precipitate a depressive episode. Efficacy data have demonstrated that both evidence-based psychotherapies and pharmacotherapies are effective treatment modalities for depression in patients with diabetes. Collaborative care has been demonstrated to be an effective health service model to deliver high quality depression care to primary care populations with comorbid depression and diabetes. New models of collaborative care are also currently being tested to integrate depression care into TEAMcare approaches to diabetes care.

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